

SUPPLEMENTAL PRELIMINARY AMENDMENT
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administering recombinant adeno-associated virus (rAAV) particles to a mammalian cell, wherein said rAAV comprise a polynucleotide encoding said therapeutic protein under control of a liver specific promoter, enhancer, or both promoter and enhancer; and wherein said rAAV provide liver specific expression of said therapeutic protein following infection of said mammalian cell.

72. The method of claim 71, wherein said administering comprises injecting said rAAV into the portal vasculature of said mammal.

73. The method of claim 71, wherein said rAAV is administered to said cell ex vivo and cells expressing said therapeutic protein are administered to said mammal.

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74. The method of claim 71, wherein said rAAV comprises two adeno-associated virus (AAV) inverted terminal repeats; wherein said inverted terminal repeats flank said enhancer, promoter or both an enhancer and a promoter, and said structural gene; and wherein said therapeutic protein is selected from the group consisting of factor VIII, factor IX and GM-CSF.

75. The method of claim 71, wherein said therapeutic protein is a diffusible polypeptide.

76. The method of claim 73, wherein said cell is a liver cell.

77. The method of claim 71, wherein said liver specific promoter or enhancer is active in hepatic cells.

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78. The method of claim 71, wherein said liver specific promoter or enhancer is selected from the group consisting of the albumin promoter, the α fetoprotein promoter, the α fetoprotein enhancer, the human apolipoprotein E (ApoE) promoter, HCR-1, HCR-2, the AI apolipoprotein liver-specific enhancer and the α 1-antitrypsin promoter.

79. The method of claim 74, wherein said therapeutic protein is GM-CSF.

80. A method of treating a liver disease or disorder in a mammal, comprising: administering a therapeutically effective dosage of recombinant adeno-associated virus (rAAV) particles to liver cells of said mammal, said rAAV particles comprising a polynucleotide encoding a therapeutic protein selected from the group consisting of factor VIII, factor IX and GM-CSF, under control of a liver specific promoter, an enhancer, or both a promoter and an enhancer, wherein the rAAV particles provide for liver specific expression of said therapeutic protein upon infection of said liver cells.

81. The method of claim 80, wherein said therapeutic protein is factor VIII and said disorder is a coagulation defect.

82. The method of claim 80, wherein said therapeutic protein is factor IX and said disorder is a coagulation defect.

83. The method of claim 80, wherein said liver specific promoter or enhancer is active in hepatic cells.

84. The method of claim 80, wherein liver specific promoter or enhancer is selected from the group consisting of the albumin promoter, the α fetoprotein promoter, the α

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fetoprotein enhancer, the human apolipoprotein E (ApoE) promoter, HCR-1, HCR-2, the AI apolipoprotein liver-specific enhancer and the α 1-antitrypsin promoter.

85. The method of claim 80, wherein said administering further comprises,

injecting said rAAV into the portal vasculature of said mammal.

86. A pharmaceutical composition for treating a liver disorder comprising,

recombinant adeno-associated virus (rAAV) particles comprising a structural gene encoding a therapeutic protein selected from the group consisting of factor VIII, factor IX, and GM-CSF;

a regulatory region for gene expression in human liver cells; and

a pharmaceutically acceptable carrier.

87. The pharmaceutical composition of claim 86, wherein said regulatory region comprises a liver specific promoter or a liver specific enhancer.

88. The pharmaceutical composition of claim 87, wherein said liver specific enhancer or promoter is active in hepatic cells.

89. The pharmaceutical composition of claim 87, wherein said liver specific promoter or enhancer is selected from the group consisting of the albumin promoter, the α fetoprotein promoter, the α fetoprotein enhancer, the human apolipoprotein E (ApoE) promoter, HCR-1, HCR-2, the AI apolipoprotein liver-specific enhancer and the α 1-antitrypsin promoter.